

PATENT SPECIFICATION

NO DRAWINGS

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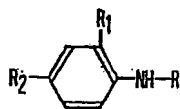
COMPLETE SPECIFICATION

Insect Control Compositions and Phenylhydrazine Derivatives therefor

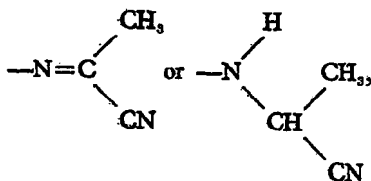
5 We, E. MERCK AKTIENGESELLSCHAFT, a German Body Corporate of Frankfurterstrasse 250, Darmstadt, Germany, do hereby declare the invention, for which we pray that a patent may be granted to us, and the method by which it is to be performed, to be particularly described in and by the following statement:—

10 The present invention is concerned with insect control compositions and with phenylhydrazine derivatives suitable for use in such compositions and processes for the preparation of such derivatives.

15 We have found that phenylhydrazine derivatives of the formula



wherein R is



20 R_1 is H and R_2 is H or halogen or R_1 and R_2 are NO_2 , and their salts are active against harmful insects and their development stages that damage crop plants by eating them. These include, for example, various imagoes

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and insect larvae, particularly beetles and caterpillars. These compounds prevent severe damage caused by these insects feeding on the vegetative organs, buds and fruits of annual and perennial crop plants. After a latent period, they lead, through symptoms that indicate narcotizing or paralysing effects, to the elimination or killing of the insects in question. The compounds of formula I and their salts are particularly remarkable for their specific activity, which enables them to be used against certain pests, while parasites and animals that prey on them are not affected.

The present invention accordingly comprises insect control compositions comprising one or more compounds of formula I and/or salts thereof and a liquid or solid diluent or carrier.

Formula I includes, for example, the following compounds: cis- and trans-acetyl cyanide phenylhydrazone; cis- and trans-acetyl cyanide - *p*-fluorophenylhydrazone, and the corresponding chlorine, bromine and iodine derivatives; cis- and trans-acetyl cyanide - 2,4 - dinitrophenylhydrazone; α -phenylhydrazino - propionitrile; α -[*p*-fluorophenylhydrazino] - propionitrile and the corresponding chlorine, bromine and iodine derivatives; and [2,4 - dinitrophenylhydrazino]-propionitrile.

Compounds of formula I in which R is $-\text{NH}-\text{CH}(\text{CH}_3)\text{CN}$ form salts, for example sulphates or hydrohalides, such as hydrochlorides or hydrobromides, with acids, particularly with strong mineral acids. These salts may be used as active substances, like the corresponding basic compounds of formula

I, in the pest control compositions according to the invention. A mixture of several compounds of formula I and/or their salts may also be used, if desired, in an insect control composition according to the invention, particularly mixtures of cis-isomers and trans-isomers.

The active substances are applied in the usual forms for insect control compositions, for example in the form of solutions, emulsions, suspensions or dusting agents. The insect control compositions according to the invention generally contain the active substance(s) in a proportion of from 5 to 95% by weight, and preferably from 20 to 80% by weight. Any of the conventional diluents and carriers for insect control compositions can be used in the compositions according to the invention.

Thus, for example, the active substances of formula I and/or their salts may be used in the form of suspensions, emulsions or solutions together with a suitable liquid carrier, for example an inert organic solvent, such as benzene, toluene, xylene or other suitable hydrocarbons or their mixtures, or, preferably, with water, for example in aqueous suspension. The active substances may also be used together with a powdered carrier, for example with powdered silicates, such as mica, bole, talcum or clay, or other inert solid powdered compounds so as to form a dusting agent.

If necessary, the solution, suspension or emulsion is prepared with the use of a solubilizer or emulsifier. Suitable surface active agents are used for this purpose. Surface active agents that bring about better adhesion of the dusting agent to the plants treated with it may also be added to a powdered preparation. A suspension can easily be prepared at the time of use, if desired, from a powdered mixture containing a surface active agent. Anionic, cationic or non-ionic surface active agents may be used. The following compounds, for example, are suitable for this purpose:—

Soaps such as sodium laurate; alkyl sulphates or alkyl sulphonates, such as sodium dodecyl sulphate or sodium dodecyl sulphate; sulphonated and sulphated ethers; sulphonated alkyl fatty acid esters; sulphonated glycol fatty acid esters; quaternary ammonium salts, such as trimethyl ammonium iodide; amines and amides with relatively long aliphatic chains; monoethers of polyglycols with long-chain aliphatic alcohols, such as the reaction products of ethylene oxide or polyethylene glycol and higher aliphatic alcohols; monoesters of polyglycols with fatty acids, for example oleic acid; monoethers of polyglycols with alkylated phenols; partially esterified polyhydric alcohols, such as sorbitan trioleate; and partially or completely esterified polyglycol ethers of polyhydric alcohols,

such as the tristearic ester of the polyglycol ether of sorbitan.

The insect control compositions are used in practice in a suitable concentration according to the age and species of the insect and the plants to be treated, climatic conditions and other factors, for example in an aqueous suspension containing 0.05 to 0.5% by weight of active substance.

Preferred active substances are compounds of formula I in which R is $-\text{N}=\text{C}(\text{CH}_3)\text{CN}$, particularly acetyl cyanide phenylhydrazone, the trans form of this compound having a particularly good action.

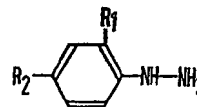
The action of the compounds of formula I and their salts has been tested as described below.

A) shoot tips of apple stocks were sprayed in the usual manner with an 0.1% emulsion of trans-acetyl cyanide phenylhydrazone (prepared by mixing a solution of 100 mg of active substance and 0.1 ml of polyoxyethylene sorbitan monooleate in 4 ml of acetone with 100 ml of water). After the emulsion had dried on the leaves, caterpillars of *Lymantria dispar* were placed on them and the leaves were then enclosed in a gauze bag. The same procedure was also carried out with unsprayed foliage as a control. In the control test, the leaves were eaten away by the caterpillars after three days, but the caterpillars did not accept the sprayed leaves and 100% of them died after seven days. The mortality in a comparative test with an 0.1% emulsion of tetranitrocarbazole, a known stomach poison, was only 50%.

B) Potato shoots were sprayed as in Test A with an 0.1% emulsion of trans-acetyl cyanide phenylhydrazone. After the coating had dried, imagoes of the Colorado beetle, *Leptinotarso decemlineata*, were placed on the shoots and they were then enclosed as in A. The same procedure was repeated with unsprayed shoots as a control. In the control test, the leaves were eaten away immediately by the beetles; the sprayed leaves were not eaten at all and were not accepted during the seven days of the test.

The compounds of formula I above in which R_1 is H and R_2 is halogen or R_1 and R_2 are NO_2 are novel compounds and they, and their salts, constitute an aspect of the present invention.

Some of the novel compounds and the other compounds of formula I can be prepared, for example, by reacting lactic acid nitrile with the corresponding phenylhydrazine of the formula



II

wherein R_1 and R_2 have the above stated meanings. It is particularly advantageous to add the lactic acid nitrile to the phenylhydrazine reactant while the latter is heated to a temperature of 60 to 180°C, preferably about 100°C. This reaction can normally be carried out without the addition of a solvent. But inert solvents, such as toluene, benzene, dimethyl formamide or water may be added. The water formed during the reaction is advantageously distilled off continuously. It is generally advisable to maintain the resulting phenylhydrazino-propionitrile for some time at an elevated temperature. It can then be recrystallized in the usual manner.

If the resulting phenylhydrazino-propionitrile is to be converted into the corresponding acetyl cyanide phenylhydrazone, oxidation (dehydrogenation) is then carried out. Suitable oxidizing agents are, for example, H_2O_2 , if desired in the presence of Fe^{++} or Fe^{+++} ions, iodine or air (advantageously in the presence of catalysts such as Fe^{++} , copper powder or iodine).

A phenylhydrazine of formula II or a salt thereof may also be reacted with acetyl cyanide in acidic solution in a polar solvent, such as water, acetonitrile, dimethyl formamide or an alcohol. If a salt of a phenylhydrazone is used as starting material, for example a nitrate, sulphate or hydrohalide (particularly hydrochloride), no further acid addition is necessary. Otherwise a mineral acid, preferably hydrochloric acid or sulphuric acid, is added.

If the compounds prepared by the above-described method have the cis-configuration, they can be converted into the corresponding trans compounds in known manner. But mixture of the cis isomer and the trans isomer can also, of course, be used in the compositions according to the invention. Isomerization can be effected by the action of known isomerization catalysts, for example in chloroform or glacial acetic acid in the presence of $AlCl_3$ or $ZnCl_2$. The solution may be heated if desired. If glacial acetic acid/ $AlCl_3$ is used, the trans compound, for example, is precipitated, while any residue of the cis compound remains in solution.

The following examples of insect control compositions according to the invention are given by way of illustration only:—

EXAMPLE 1

Emulsion concentrate

10% by weight of cis-acetyl cyanide phenylhydrazone
65% by weight of xylene
15% by weight of dimethyl formamide
10% by weight of mixed emulsifier (consisting of polyoxyethylene sorbitan ester and an alkylbenzene sulphonate) were mixed with each other to form an emulsion. The result-

ing emulsion concentrate can be used as a spraying mixture when diluted with water.

EXAMPLE 2

Spraying powder

80% by weight of trans-acetyl cyanide phenylhydrazone
0.5% by weight of a wetting agent (alkyl-naphthalene sulphonate)
10% by weight of sulphite waste liquor powder
3% by weight of silicic acid
6.5% by weight of bole
were mixed. The resulting spraying powder can be used to spray plants when suspended in water.

EXAMPLE 3

Dusting agent

2.5% by weight of acetyl cyanide-*o,p*-dinitrophenylhydrazone
96.5% by weight of talcum
1% by weight of colophony
were ground to form a homogeneous mixture. The resulting dusting agent was used directly for dusting crop plants to protect them against being eaten by insects.

The following examples illustrate the preparation of phenylhydrazines derivatives of formula I:—

EXAMPLE I

a) 108 g of phenylhydrazine were heated to about 100°C in a flask provided with a descending condenser. 71 g of lactic acid nitrile were then added drop by drop so that the reaction continued and the water formed was continuously distilled off. The whole was then heated to about 105°C for an hour and the product was then left to solidify. The crude product was recrystallized from alcohol to give about 150 g (93% of the theoretical yield) of phenylhydrazino-propionitrile, m.p. 58°C.

The following were synthesized correspondingly from the corresponding substituted phenylhydrazines.

α - (*p* - chlorophenylhydrazino) - propionitrile (m.p. 85°C);
 α - (2,4 - dinitrophenylhydrazino) - propionitrile (m.p. 189°C);
 α - (*p* - bromophenylhydrazino) - propionitrile (m.p. 98°C);
 α - (*p* - iodophenylhydrazino) - propionitrile (m.p. 94°C);
 α - (*p* - fluorophenylhydrazino) - propionitrile (m.p. 61°C).

b) 11.6 g of phenylhydrazino-propionitrile were suspended in 150 ml of 2N H_2SO_4 and 3 g of $Fe(II) SO_4$ were added; about 22 ml of H_2O_2 were then added slowly drop by drop. The reaction mixture was extracted with methylene chloride after 15 minutes. 10.3 g (90% of the theoretical yield) of a mixture of cis-acetyl cyanide phenylhydrazone

and trans-acetyl cyanide phenylhydrazone were obtained from this extract by evaporating the extraction agent. Pure cis-acetyl cyanide phenylhydrazone was obtained chromatographically after repeated recrystallization from ethanol; m.p. 74°C.

The following were obtained similarly:

cis - acetyl cyanide - 4 - bromophenylhydrazone (m.p. 152°C);

10 cis - 1 acetyl cyanide - 4 - iodophenylhydrazone (m.p. 160°C).

c) 4 g of cis-acetyl cyanide phenylhydrazone were heated to boiling for 2 hours with 10 ml of glacial acetic acid. When the solution had cooled, 2.5 g of the corresponding trans compound were precipitated; this was chromatographically pure (m.p. 150°C). A second fraction of 1.2 g of trans-acetyl cyanide phenylhydrazone slightly contaminated with cis compound (92% of the theoretical yield) was obtained by the addition of a little water to the mother liquor.

The following were obtained correspondingly:

25 trans - acetyl cyanide - 4 - bromophenylhydrazone (m.p. 185°C);

trans - acetyl cyanide - 4 - iodophenylhydrazone (m.p. 200°C).

EXAMPLE II

30 a) 61.3 g of *p*-fluorophenylhydrazine nitrate were suspended in 500 ml of acetonitrile, 22.4 g of acetyl cyanide were added drop by drop at 0°C, and the whole was stirred for 1 hour. A few drops of water were added to the now clear solution and cis-acetyl cyanide - *p* - fluorophenylhydrazone was precipitated. The yield was 44 g (76% of the theoretical yield); m.p. 121°C after recrystallization from acetonitrile.

40 The following were prepared similarly from the corresponding phenylhydrazine nitrates. cis - acetyl cyanide - *p* - chlorophenylhydrazone (m.p. 136°C) and

45 acetyl cyanide - 2,4 - dinitrophenylhydrazone (m.p. 140°C).

b) 12 g of cis-acetyl cyanide-*p*-fluorophenylhydrazone were dissolved in 60 ml of glacial acetic acid and 2 to 4 g of AlCl₃ were added. Water was added after 15 minutes and the corresponding trans compound, which precipitated in an oily form, was taken up in methylene chloride. 9 g of crystalline trans-acetyl cyanide - *p* - fluorophenylhydrazone (75% of the theoretical yield) were obtained from this extract; this compound melted at 148°C after recrystallization from acetonitrile.

The following were prepared similarly:

60 trans - acetyl cyanide *p* - chlorophenylhydrazone (m.p. 171°C).

The salts of the compounds of formula I in which R represents —NH—CH(CH₃)CN were obtained in the usual manner by reacting the compounds with the correspond-

ing acids, for example by introducing HCl gas into an ethereal solution of a compound of formula I.

The following may be mentioned as examples:

The hydrochlorides of:

α - phenylhydrazino - propionitrile (m.p. 161°C);

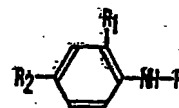
α - (*p* - fluorophenylhydrazino) - propionitrile (m.p. 188°C);

α - (*p* - chlorophenylhydrazino) - propionitrile (m.p. 165°C);

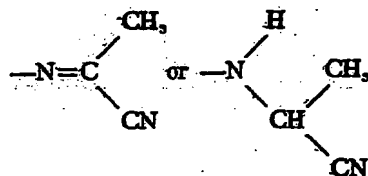
α - (*p* - bromophenylhydrazino) - propionitrile (m.p. 145°C).

WHAT WE CLAIM IS:—

1. An insect control composition comprising one or more phenylhydrazine derivatives of the formula



wherein R is

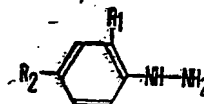


R₁ is H and R₂ is H or halogen or R₁ and R₂ are NO₂, and/or salts thereof, and a liquid or solid diluent or carrier.

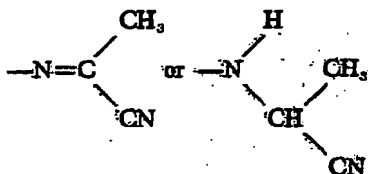
2. An insect control composition which comprises acetyl cyanide phenylhydrazone and a liquid or solid diluent or carrier.

3. An insect control composition substantially as herein described in any of Examples 1 to 3.

4. A phenylhydrazine derivative of the formula

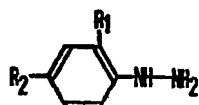


wherein R is



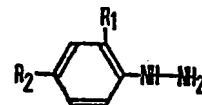
and R_1 is H and R_2 is halogen or R_1 and R_2 are NO_2 , or a salt thereof.

5. Acetyl cyanide - *o,p* - dinitrophenylhydrazones.
- 5 6. Acetyl cyanide - *p* - halophenylhydrazones.
7. Acetyl cyanide-*p*-fluorophenylhydrazones.
8. Acetyl cyanide-*p*-chlorophenylhydrazones.
9. Acetyl cyanide-*p*-bromophenylhydrazones.
- 10 10. Acetyl cyanide-*p*-iodophenylhydrazones.
11. α - (*p* - Fluorophenylhydrazino) - propionitrile.
12. α - (*p* - Chlorophenylhydrazino) - propionitrile.
- 15 13. α - (*p* - Bromophenylhydrazino) - propionitrile.
14. α - (*p* - Iodophenylhydrazino) - propionitrile.
- 20 15. α - (2,4 - Dinitrophenylhydrazino) - propionitrile.
16. A process for the preparation of a phenylhydrazine derivative of the formula specified in claim 1, which comprises reacting lactic acid nitrile with a phenylhydrazine of the formula
- 25



fied in claim 1, at a temperature of from 60° to 180°C. while removing the water formed by the reaction and, if desired, treating the product obtained with an oxidising agent.

17. A process for the preparation of a phenylhydrazine derivative of the formula specified in claim 1, which comprises reacting a phenylhydrazine of the formula



II
wherein R_1 and R_2 have the meanings specified in claim 1, or an acid addition salt thereof, with acetyl cyanide in acidic solution in the presence of a polar solvent.

18. A process according to claim 16 or 17, in which the *cis*- product obtained is isomerized in acid solution to form the corresponding *trans*-compound.

19. A process for the preparation of a phenylhydrazine derivative of the formula specified in claim 1 substantially as herein described in Example I or II.

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wherein R_1 and R_2 have the meanings speci-

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